

## 32 THE EFFECT OF ACUTE AND REPEATED NICOTINE INJECTIONS ON BRAIN DOPAMINE ACTIVATION: COMPARISONS WITH MORPHINE AND AMPHETAMINE.

P. Vezina, D. Hervé, J. Glowinski and J.-P. Tassin.

Chaire de Neuropharmacologie, INSERM U.114,  
Collège de France, 75231 Paris Cedex 05, France.

Acute systemic injections of morphine, amphetamine and nicotine elicit increased locomotion in rats and repeating these injections produces an enhanced or sensitized locomotor effect. Different lines of evidence suggest that mesolimbic dopamine (DA) activation underlies the acute locomotor effects of these drugs and that enhanced activity in this system is responsible for sensitization to the locomotor effects of morphine and amphetamine. Relatively little is known, however, about the effects on DA activation of repeated injections of nicotine.

We have found that acute injections of (-)-nicotine bitartrate (0.4-0.8 mg/kg, base, s.c.) produce substantial increases (41-49%) in DOPAC/DA in the nucleus accumbens (N.Acc.) and more moderate increases (26-37%) in the antero-medial striatum. Surprisingly, repeating these injections reduced (to 15-26% in N.Acc.) or abolished (in antero-medial striatum) these increases in DA turnover. Interestingly, the opposite effect was obtained in the medial prefrontal cortex (mPFC). Small increases in DOPAC/DA produced by acute injections (18%) gave way to larger increases (31%) after repeated injections. In comparison, acute morphine produced large increases in DOPAC/DA in the N.Acc. (59%) and the mPFC (61%). Unlike with nicotine, however, repeating these injections substantially enhanced the effect of morphine in the N.Acc. (96%) but slightly reduced it in the mPFC (52%).

These findings suggest that nicotine differs from morphine (and amphetamine) in the manner in which it produces enhanced locomotor effects following repeated injection and possibly in its relation to DA as a mediator of reward. Indeed, repeated nicotine reduces the acute activating effects of this drug in subcortical DA terminal fields and increases it in the mPFC while repeated morphine increases these effects in subcortical sites and produces small decreases or no changes in the mPFC.

Results from further experiments suggest that the differential effects of these drugs on DA activation may also have consequences on the regulation of mu-opiate receptors in subcortical DA terminal fields. Preliminary results obtained by quantitative autoradiography indicate that mu-opiate binding sites in these areas are upregulated following repeated injections of amphetamine but not of nicotine. These effects may be related to the sensitization of subcortical DA function induced by repeated amphetamine (and morphine) but not by nicotine.

2021546640